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File: USPT

Oct 26, 1999

DOCUMENT-IDENTIFIER: US 5972612 A

TITLE: Surface-sensitive detection of hybridization at equilibrium

Brief Summary Text (6):

Sequencing by hybridization (SBH) (see e.g. Drmanac et al., Genomics 4: 114; Strazoski et al., Proc. Natl. Acad. Sci. USA 88: 10089 (1991); Bains and Smith, J. Theoretical Biol. 135: 303 (1988); and U.S. Pat. No. 5,202,231) has become an interesting alternative to traditional sequencing with a potential for higher through-put of information. This type of system utilizes the information obtained from multiple hybridizations of the polynucleotide of interest, using short oligonucleotides to determine the nucleic acid sequence. However, there are several technical problems associated with this technology. For example, while today there are ways to build arrays of oligonucleotides on a chip based on the synthesis of oligoprobes and photolithographic techniques, it is still complicated to provide on a chip the large set of oligonucleotide probes required for determining a random nucleic acid sequence. Further, the detection of interaction of labelled target DNA is normally done by fluorescent or radioactivity measurements. Such detection is dependent on washing of the chip to get rid of residual labelled target molecules and the oligoprobes must therefore bind rather strongly to the target molecules. There are also problems with the binding of oligoprobes with a single base mismatch in combination with the different sensitivity to washing conditions dependent on base pair composition, G:C being more stable than A:T. One attempt to overcome such problems is to use tetraalkylammonium salts that eliminate the difference in stability of G:C and A:T base pairs.

Brief Summary Text (29):

The present invention thus relates to the analysis of the interaction between a first nucleic acid and a complementary second nucleic acid under annealing conditions where high kinetic (dissociation rate) constants are present in the interaction and equilibrium of the reaction therefore can be achieved rapidly, i.e. that the reaction will readily reach equilibrium within a reasonable time during the experiment. This is valid for the formation of e.g. DNA--DNA dimers as well as sequence dependent formation of other complexes of nucleic acids.

Brief Summary Text (53):

Among optical methods may particularly be mentioned those that detect surface refractive index, such as reflection-optical methods, including both internal and external reflection methods, e.g. ellipsometry and evanescent wave spectroscopy (EWS), the latter including surface plasmon resonance spectroscopy (SPRS), Brewster angle refractometry, critical angle refractometry, frustrated total reflection (FTR), evanescent wave ellipsometry, scattered total internal reflection (STIR), optical wave guide sensors, evanescent wave based imaging, such as critical angle resolved imaging, Brewster angle resolved imaging, SPR angle resolved imaging, etc., as well as methods based on evanescent fluorescence (TIRF) and phosphorescence.